CHEST

Lung Imaging in COPD Part 1
Clinical Usefulness

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COPD is a condition characterized by chronic airflow obstruction resulting from chronic bronchitis, emphysema, or both. The clinical picture is usually progressive with respiratory symptoms such as exertional dyspnea and chronic cough. For many years, spirometry was used to establish a diagnosis of COPD. Recent advancements in imaging techniques allow quantitative and qualitative analysis of the lung parenchyma as well as related airways and vascular and extrapulmonary manifestations of COPD. These imaging methods may allow prognostication of disease and shed light on the efficacy of pharmacologic and nonpharmacologic interventions. This is the first of a two-part series of articles on the usefulness of imaging methods in COPD, and it highlights useful information that clinicians can obtain from these imaging studies to make more accurate diagnosis and therapeutic decisions. CHEST 2023; 164(1):69-84

KEY WORDS: CT scan of chest; chest CT scan; COPD; emphysema; comorbidities associated with COPD; extra-pulmonary manifestations of COPD

FOR EDITORIAL COMMENT, SEE PAGE 8

As early as the 17th century, autopsy reports of COPD described hyperinflated lungs that did not empty well.[1] Although spirometry was invented in the mid 19th century, it was not until the mid 20th century that airflow obstruction was measured objectively. The gold standard measurements of FEV_1 and FEV_1 to FVC ratio were introduced to clinical medicine for diagnosis and prognosis in the early 1950s. The definition of COPD based on the Global Initiative for Chronic Obstructive Lung Disease guidelines requires an FEV_1 to FVC ratio of < 0.7. Because this ratio declines with age, it has been advocated to use the fifth percentile of the lower limit of normal of the FEV_1 to FVC ratio to define true airways obstruction.[2]

Patients with risk factors for COPD (tobacco use) and normal spirometry values (FEV_1 to FVC ratio > 0.70 and $FEV_1 > 80\%$ predicted) have not been considered to have COPD, despite suggestive findings on CT scan imaging. The Genetic Epidemiology of COPD (COPDGene) Study in 2015 reported that 54% of this group showed one

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or more findings suggesting COPD, such as dyspnea; shorter 6-min walk distance; a reduced respiratory quality of life; or a CT scan showing emphysema, gas trapping, or airway disease.[3] Imaging findings in this group showed that 32% demonstrated airway wall thickening and 10% demonstrated emphysema on quantitative analysis of CT scans. A recent publication by the Lancet Commission on COPD[4] suggested that chest CT scans should be reviewed for COPD, including early abnormalities. The authors proposed a broader definition of COPD and that CT scan-detected emphysema, air trapping, and airway remodeling be considered diagnostic of COPD, even in the absence of airways obstruction on spirometry. If these recommendations become widely accepted, lung imaging will have a greater importance in the early detection of COPD and possible prevention of disease progression.

Examples of when chest imaging may have particular usefulness include assessing patients with dyspnea and normal spirometry findings when chest imaging may show significant emphysema. Also, patients with mild obstruction on spirometry may show distinct abnormalities in chest CT scans such as mucus plugging, combined pulmonary fibrosis and emphysema, and clues to pulmonary hypertension. These additional findings may explain why such patients have frequent exacerbations or are symptomatic beyond the extent of obstruction on spirometry. Chronic bronchitis is a clinical diagnosis and is defined as chronic productive cough for 3 months in each of 2 consecutive years. Emphysema is an anatomic diagnosis and is defined as abnormal, permanent dilation and destruction of the distal airspaces, and its presence on CT scan imaging can identify people at greatest risk of an accelerated loss of lung function.[5]

Patients with COPD are a heterogeneous group, and advances in CT scan imaging technology over the past 40 years have made this visually apparent. Newer techniques assessing lung structure have provided qualitative and quantitative metrics that show distinct parenchymal, airway, vascular, and extrapulmonary manifestations of COPD. Improved characterization of COPD imaging traits is having considerable impact on the diagnosis and management of COPD as this knowledge is brought to clinical practice (Table 1). Disease detection, stratification, and subtyping are well-accepted applications of CT scan imaging in clinical management and research. It is increasingly clear that

TABLE 1] Role of Chest CT Scan Imaging in the Clinical Management of COPD

Role	Purpose	Examples
Diagnosis, severity, and disease manifestations	Identify pulmonary and extrapulmonary conditions that may be responsible for the patient's clinical presentation	Emphysema, bronchiectasis, tracheobronchomalacia, pulmonary hypertension, and cardiac conditions
Subtyping	Determine pulmonary and extrapulmonary features that are associated with subtypes of COPD	Emphysema classification and location, airway abnormalities, gas trapping, and giant bullae
Comorbidities	Assess pulmonary and extrapulmonary conditions that may require specific intervention	Pulmonary hypertension, heart failure, lung cancer, tobacco use-related interstitial fibrosis, interstitial lung abnormalities, combined pulmonary fibrosis and emphysema, bronchiectasis, osteoporosis or fractures, sarcopenia, saber-sheath trachea
Clinical management	Identify features that assist in disease management	Emphysema severity and distribution—lung volume reduction surgical and nonsurgical; complete interlobar fissures for nonsurgical volume reduction, lung cancer
Prognostication	Determine imaging features associated with clinical course	Exacerbation risk—pulmonary artery to aortic ratio > 1, mortality—emphysema presence and severity
Research	Assess presence, severity, and course of imaging abnormalities that lead to understanding of biologic mechanisms and clinical course of disease	Quantitative emphysema, parametric response mapping

TABLE 2] Radiologic and Clinical Features of COPD Comorbidities

Comorbidities	Radiologic Features	Clinical Features
Lung cancer	Radiographic features of emphysema and air trapping and the severity of airflow obstruction are risk factors for lung cancer and cancer mortality.	The USPSTF states with moderate certainty that annual screening for lung cancer with low-dose CT scan has a moderate net benefit in people at high risk (age, total cumulative tobacco use exposure, and years since quitting).
PH	Chest radiography may provide clues to the presence of PH with dilatation of the pulmonary artery. On CT scan, the ratio of the main PA to ascending aorta diameter > 1.0 may predict PH.	Transthoracic echocardiography is the initial test of choice but may not be accurate due to lung hyperinflation. It estimates systolic PA pressure and evaluates hypertrophy and dilatation of the right ventricle. Right heart catheterization confirms the diagnosis.
Bronchiectasis	Radiological criteria are broncho-arterial ratio >1, lack of bronchial tapering, and visualization of peripheral bronchi within 1 cm of the pleural surface	Patients have greater sputum production, higher inflammatory biomarkers, worse airflow obstruction, and higher exacerbation rates. Colonization with potentially pathogenic organisms such as *P aeruginosa.*
ILA	Often incidentally detected on chest CT scan imaging and seen with emphysema. Fibrotic ILA with traction bronchiectasis has worse prognosis.	ILAs may be independent predictors of mortality; 50% will progress over 5 years. Follow-up needed to evaluate for progressive physiologic or symptomatic impairment.
Tobacco use-related interstitial fibrosis or airspace enlargement and fibrosis	These are overlapping histologic terms indicating the presence of fibrosis in individuals who smoke cigarette. Radiologic findings include centrilobular nodularity, ground-glass abnormality, and cysts.	Occurs in individuals who use tobacco; 5-y survival high, most are asymptomatic.
CPFE	The presence of emphysema predominantly in the upper lobes and parenchymal fibrosis in the lower lobes on CT scan imaging	CPFE predisposes to lung cancer and pulmonary hypertension and is associated with relatively high mortality. A low D_{LCO} and severe exercise hypoxemia are found often with mild spirometry changes.
Coronary artery disease	Coronary calcifications seen on CT scans.	Validated risk assessment for coronary artery disease
Osteoporosis	Osteoporosis, vertebral fractures, and degenerative spine disease may be detected on chest CT scan imaging and often are underreported.	Preventive measures for low bone mineral density and vertebral fractures are needed for many patients with COPD.
Pulmonary cachexia	CT scan imaging provides a noninvasive means of assessing skeletal muscle bulk.	Reduced muscle size is associated with poorer clinical outcomes.

CPFE = combined pulmonary fibrosis with emphysema; D_{LCO} = diffusing capacity of the lungs for carbon monoxide; ILA = interstitial lung abnormality; PA = pulmonary artery; PH = pulmonary hypertension; USPSTF = United States Preventive Services Task Force.

these imaging features also can be used for prognostication and detection of comorbidities associated with COPD (Table 2). These radiologic features of COPD will be discussed in this and a subsequent *CHEST* article entitled "Lung Imaging in COPD Part 2: Emerging Concepts."[6]

Methods

Evidence Used in This Review

We conducted a targeted search of PubMed/MEDLINE, Web of Science, and Google Scholar from January 1, 2000, through March 30, 2022, for randomized controlled trials, observational studies, scoping reviews, systematic reviews, meta-analyses, and clinical practice guidelines. We searched for the terms *chronic obstructive pulmonary disease*, *COPD*, and *imaging*. We further enhanced our search by evaluating the reference lists of selected articles and supplemented our search with literature from our own collections.

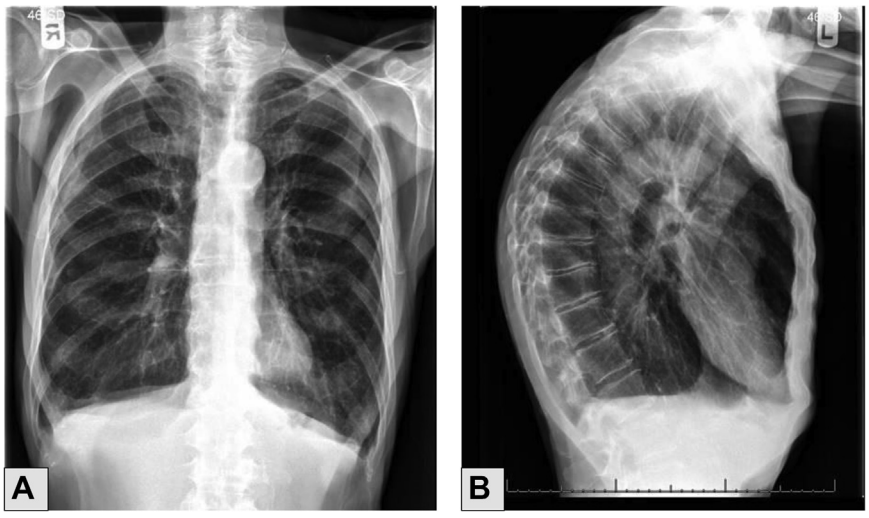

Figure 1 – *A, B, Posteroanterior (A) and lateral (B) chest radiographs from a patient with emphysema showing increased lucency of the lungs with pruning of the peripheral vasculature, flattening of the diaphragms, increased retrosternal space, widening of the intercostal spaces, kyphosis (barrel-shaped chest), and a narrowed cardiac silhouette.*

A detailed description of the methodology used for searching articles is included in e-Figure 1.

Imaging Techniques

The appropriate initial imaging study for patients with dyspnea with suspected COPD is chest radiography (CXR), which can evaluate findings suggestive of COPD and alternative diagnoses.[7] Using an algorithmic approach, the combination of CXR, pulmonary function, and selected blood tests resulted in a specific diagnosis in one-third of patients with chronic dyspnea.[8] Another study reported that 14% of chest radiographs ordered during COPD evaluation detected potentially treatable causes of dyspnea other than COPD and lung cancer, and that 84% of radiographs assisted in management.[9]

Posteroanterior and lateral CXR at full inspiration are a standard part of the clinical evaluation of patients with COPD. CXR is inexpensive, easily obtained, and involves minimal radiation exposure. CXR findings that suggest emphysema include hyperlucent lung fields, diaphragm flattening, vascular pruning, increased retrosternal airspace, widening of the intercostal spaces, and a narrowed and more vertical cardiac silhouette (Fig 1).[10] Using a combination of these criteria, CXR has yielded a sensitivity of 90% and a specificity of 98% for emphysema, although CXR generally is insensitive for diagnosing the earliest stages of emphysema.[11] Chronic bronchitis is a clinical, rather than a radiologic, diagnosis; CXR findings including increased bronchovascular markings are nonspecific. Occasionally, abnormally thickened airway walls can be identified when bronchi lie in the appropriate plane, as occurs in the anterior segment of the right upper lobe.[12] Innovations in CXR include dark-field radiographic imaging and dynamic radiography for pulmonary functional imaging, but further investigations are needed to establish their usefulness in the evaluation of COPD.[13,14]

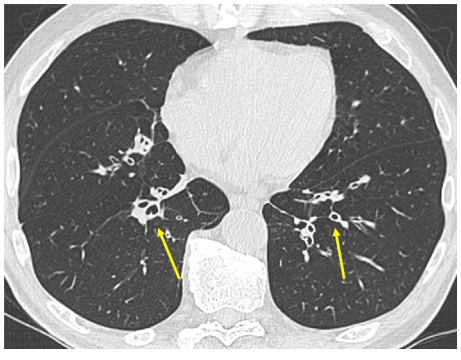

Figure 2 – *Axial CT scan image showing chronic bronchitis. Bronchial wall thickening is present bilaterally (arrows).*

CT scan imaging is the most widely available and precise imaging method for the characterization of COPD, with a greater sensitivity and specificity than CXR in determining the type, extent, and distribution of emphysema and bronchial abnormalities.[15] Unenhanced low-dose chest CT scan imaging is recommended for initial COPD characterization, subtyping, and evaluation of other pulmonary and extrapulmonary manifestations.[16] The recommended scanning protocol includes volumetric full chest scanning in the supine position at full inspiration, with slice thickness of 1 to 1.25 mm, and reconstructed with a high spatial frequency or sharpening algorithm.[15] However, a smooth reconstruction algorithm is recommended for quantitative CT scan measurements. In addition to the thin-slice axial images, coronal and sagittal reformatted images and maximum intensity projection images should be obtained to carry out a more complete evaluation of abnormal findings, especially lung nodules. Minimum intensity projection images may help to show the presence and extent of emphysema. Clinically, low attenuation of the lung parenchyma detects emphysema. Quantitative CT scan detection uses pixels of ≤ -950 HU or being in the lower 15 percentile of the CT scan histogram (see part 2 of this series[6]). Airway disease may manifest as bronchial wall thickening, bronchiectasis, centrilobular nodules, air trapping, or a combination thereof. Routine end-expiratory imaging is used to assess regional air trapping and can help to determine the presence or severity of airway obstruction, or both and to identify less common causes of airway obstruction such as hypersensitivity pneumonitis or obliterative bronchiolitis. Dynamic expiratory imaging, with images obtained during forced expiration, is most useful to assess dynamic narrowing of the airways as in tracheobronchomalacia.[17]

Contrast-enhanced CT scan pulmonary angiography (CTPA) may play a role in the evaluation of patients who seek treatment at a hospital with COPD exacerbations, because pulmonary embolism may contribute to acute worsening of respiratory symptoms in these patients.[18] CTPA is the first-choice diagnostic imaging method in patients with suspected pulmonary embolism because it is both sensitive and specific. The imaging technology is widely available and can be performed on an emergent basis. CTPA examination

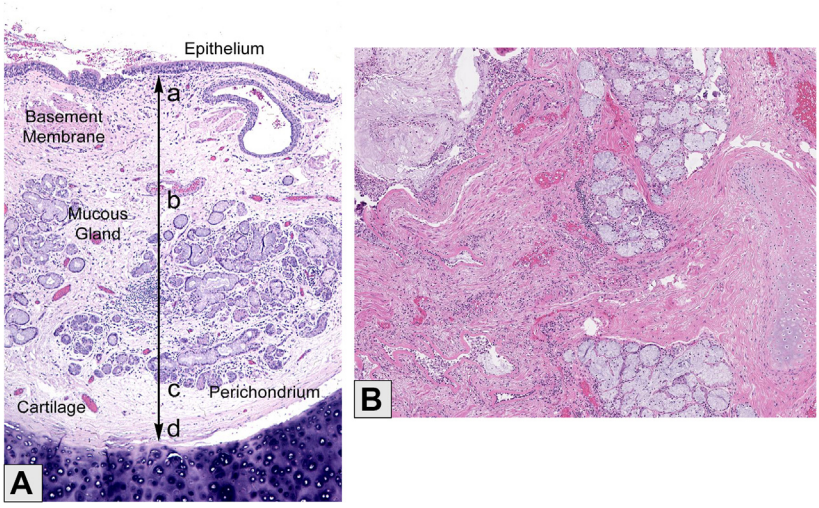

Figure 3 – *Photomicrographs utilizing hematoxylin and eosin stains showing chronic bronchitis according to the Reid index. A, Hyperplastic mucous glands constitute > 50% of the thickness of the bronchial wall (original magnification, ×1). The Reid index equals the maximum thickness of the bronchial mucous glands internal to the cartilage (b to c) divided by the bronchial wall thickness (a to d). B, Bronchial wall pathologic features in chronic bronchitis (original magnification, ×4). The wall of this bronchus between the cartilage (far right) and the mucosa (top left) shows marked thickening by bronchial submucosal glands, smooth muscle, fibrosis, and chronic inflammation. In addition, obstruction of the bronchial lumen by mucous is present. (Figure 3A reproduced, with permission, from Travis WD, Colby TV, Koss MN, et al. Non-neoplastic Disorders of the Lower Respiratory Tract,* Atlas of Nontumor Pathology. *Series 1, Volume 2. American Registry of Pathology; 2002).*[29]

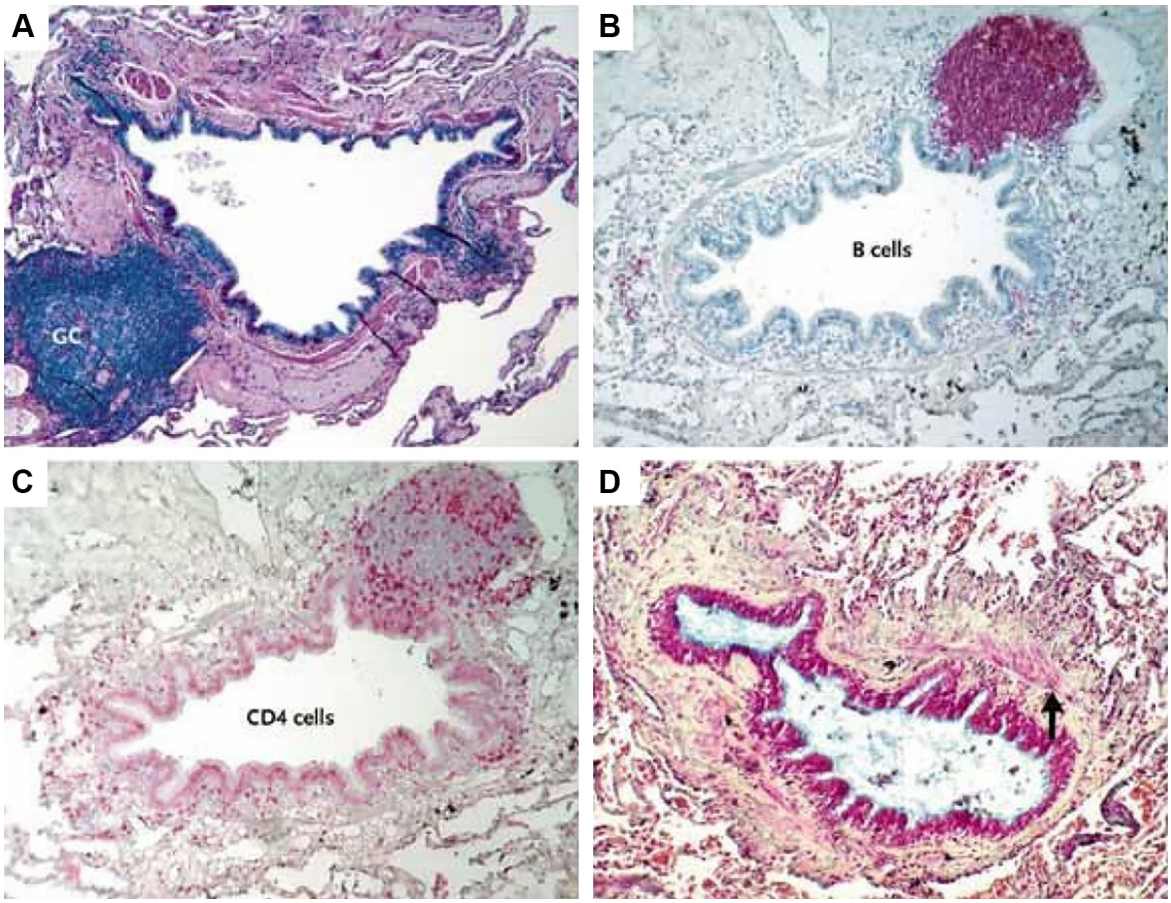

Figure 4 – *Photomicrographs showing pathologic findings in COPD. A, Collection of bronchial lymphoid tissue with a lymphoid follicle containing a GC surrounded by a rim of darker-staining lymphocytes that extend to the epithelium of both the small airways and alveolar surface (Movat stain; original magnification, ×10). B-D, Another follicle, in which the GC stained strongly for B cells (B) and a serial section of the same airway stained for CD4 cells (CD20 stain; original magnification, ×10) (C), which are scattered around the edge of the follicle and in the airway wall (CD4 stain; original magnification, ×10). An airway that has been remodeled extensively by connective tissue deposition in the subepithelial and adventitial compartments of the airway wall (D). The arrow points to the smooth muscle that separates the subepithelial from the adventitial compartments (Movat stain; original magnification, ×20). GC = germinal center. Reprinted with permission from New England Journal of Medicine, Hogg, JC, et al, The Nature of Small-Airway Obstruction in Chronic Obstructive Pulmonary Disease. Figure 2 Volume 350, p 2649. Copyright © 2004, Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.*[28]

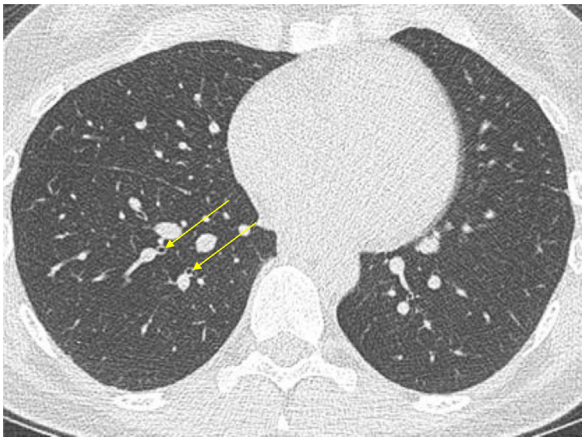

Figure 5 – *High-resolution CT scan section through the lower lobes showing diffuse narrowing of the basilar airways (arrows) resulting from asthma. Note marked disparity of airway appearance when compared with adjacent pulmonary artery branches.*

should be performed on a multidetector CT scan imaging scanner and requires thin-section (< 2.5 mm) volumetric images of the chest after the bolus administration of IV contrast that is timed precisely to optimize enhancement of the pulmonary arteries. Alternative diagnoses also may be discovered using this method.[19] CTPA also can detect pulmonary hypertension (PH), including identification of pruning of the peripheral pulmonary vasculature, a common complication of COPD, in addition to providing clues as to the cause of PH.[20]

CT Scan-Definable Subtypes

Chronic bronchitis represents a CT scan-definable subtype of COPD distinct from emphysema and small airways disease.[15,21] CT scan findings associated with chronic bronchitis primarily rely on identification of abnormal bronchial wall thickening (Fig 2). Bronchial wall thickening may reflect any combination of airway remodeling, mucus gland hypertrophy, excessive mucus secretions, smooth muscle hyperplasia, encroachment from epithelial thickening, and destroyed alveolar attachments.[22] These findings lead to increased airflow resistance, most often secondary to increased luminal mucous production related to underlying airway inflammation induced by tobacco use (Fig 3). In COPD, the airways can be altered by inflammation, remodeling, and narrowing of the bronchioles leading to increased airflow resistance. Historically, emphasis was made on the large airways where the Reid index was used to measure the thickness of the bronchial mucous glands.[23,24] However, this finding is not always related to airflow obstruction, and the primary reason for airflow obstruction associated with large airway pathologic features is increased luminal mucous production. The underlying cause is airway inflammation in response to injury induced by tobacco use.

Small airways measuring < 2 mm are thought to be the primary site of lung injury and airflow obstruction in COPD.[25,26] Mucous plugging, narrowing, and obliteration of membranous and respiratory bronchioles are thought to be the result of inflammation.[27] This leads to epithelial injury, resulting in goblet cell metaplasia, luminal inflammatory mucous exudates, and an increase in volume of tissue in the wall.[28] Respiratory bronchiolitis with intralumenal pigmented macrophages and bronchiolar chronic inflammation, fibrosis, or both is an early manifestation of bronchiolar injury caused by tobacco use, and these changes may be detected by lung imaging (Fig 4).

Detecting bronchial narrowing by using the bronchial to arterial ratio is not reliable because of normal variations in this measurement.[29,30] Technical variables that can lead to overdiagnosis of airway wall thickening may include submaximal inspiration, narrow window settings, and edge-enhancing reconstruction algorithms. Bronchial wall thickness increases with age. Bronchial wall thickening also may occur in asthma (Fig 5),[31] infection (Fig 6), or microaspiration.[21] Abnormal peribronchial interstitium (for example, with pulmonary edema or sarcoidosis) may simulate bronchial wall thickening. Although standard reference images have been published,[22,32] assessment of airway wall thickness remains subjective, with only fair to moderate interobserver variability at best.

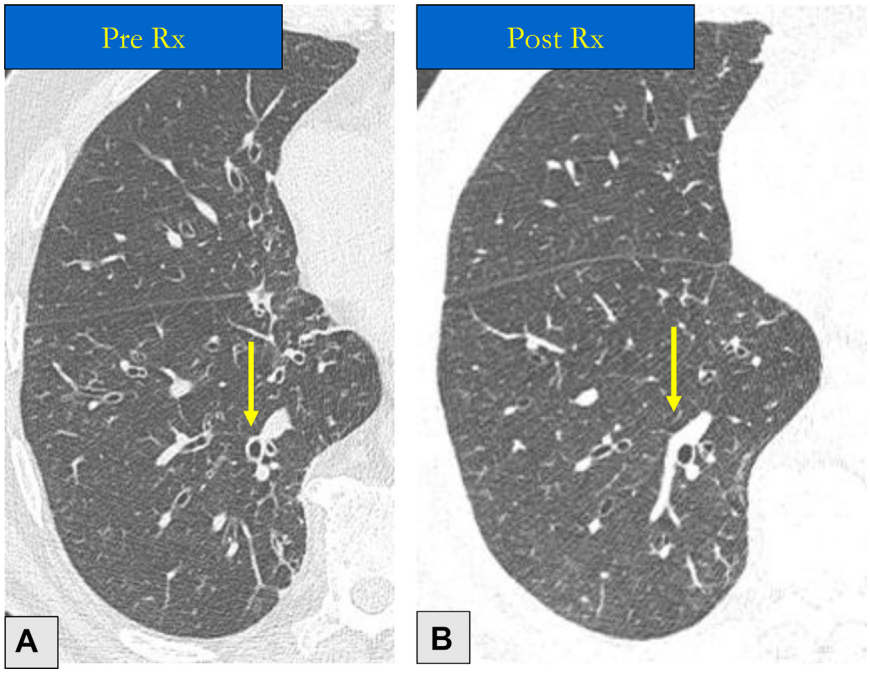

Figure 6 – *A, B, Coned-down high-resolution CT scan images through the middle and right lower lobes showing reversible airway wall changes resulting from infection: diffuse bronchial wall thickening is present before antibiotic therapy (arrow in A) that resolved after therapy (arrow in B).*

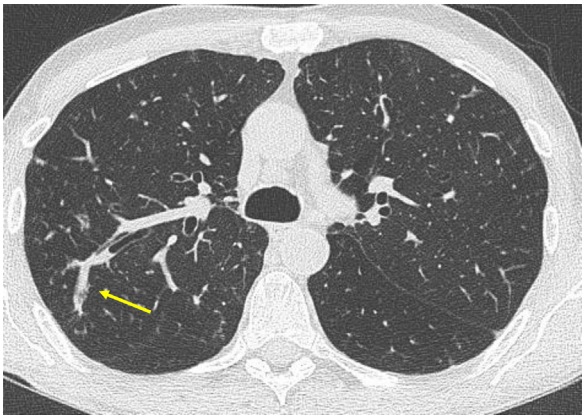

Figure 7 – *High-resolution CT scan section through the carina showing bronchiectasis and focal mucoid retention associated with chronic bronchitis in the posterior segment of the right upper lobe (arrow). Note mild diffuse proximal airway dilatation associated with mild hyperinflation.*

Despite these limitations, visual CT scan evaluation of the airways is helpful in COPD for several reasons. Bronchial wall thickening on CT scan imaging may suggest an asthmatic component of COPD.[28] However, it also may be seen in individuals who use tobacco and during COPD exacerbations.[33,34] Mucus plugging on CT scan imaging (Fig 7) increasingly is recognized as an important marker of chronic bronchitis and is associated with airflow obstruction, more frequent exacerbations, and impaired quality of life.[32,35,36] Additionally, CT scan imaging can identify alternative causes of symptoms such as bronchiectasis[37,38] as well as comorbid abnormalities such as pulmonary hypertension, coronary artery disease, vertebral fractures, diminished muscle mass, and obesity.[39]

Emphysema is a readily recognizable feature of COPD on CT scan imaging. It may be classified radiologically as centrilobular, panlobular, and paraseptal, and this distinction may suggest the cause of the emphysema.[40] Centrilobular emphysema (CLE) is recognized by the presence of well-defined round lucencies of varying size, sometimes associated with a visible central artery (Fig 8). CLE may be graded as trace (occupying < 0.5% of a lung zone), mild (occupying 0.5%-5% of a zone), moderate (occupying > 5% of any zone), confluent (coalescent lucencies spanning several lobules), or advanced destructive (coalescent lucencies with hyperexpansion of lobules and architectural distortion) (Fig 9).[15] Paraseptal emphysema is another morphologic subtype of emphysema that is peripheral and subpleural and comprises focal lucencies that can be relatively large (Fig 10). CLE severity is an independent prognostic marker for mortality and for lung cancer risk.[41,42] Additionally, progression of emphysema on quantitative CT scan imaging is greater in those with higher degrees of CLE at baseline.[43]

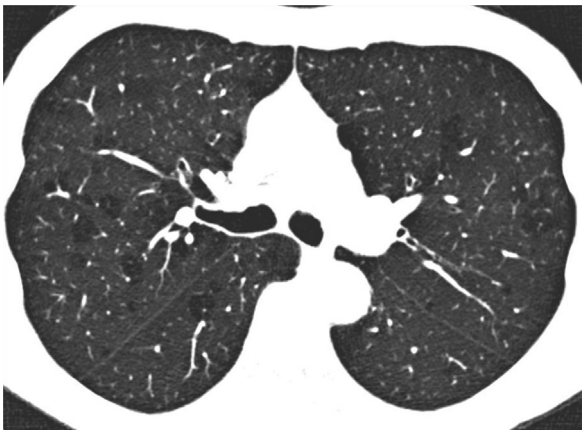

Figure 8 – *Axial thin-section CT scan image showing centrilobular emphysema with multiple well-defined lucencies of varying size without appreciable walls and some with a visible central artery.*

Panlobular emphysema, unlike CLE, involves the entire pulmonary lobule, resulting in diffuse decrease in attenuation and decreased vascularity (Fig 11). Confluent emphysema or advanced destructive emphysema are preferable terms when describing tobacco use-related emphysema.[15] Although panlobular emphysema may be found in advanced tobacco use-related emphysema, this term generally is reserved for individuals with α_1-antitrypsin deficiency. The panlobular emphysema of α_1-antitrypsin deficiency typically involves all lobes, with some lower lung predominance and associated linear abnormalities in the lower lungs.[44]

Paraseptal emphysema is characterized by subpleural cystlike lucencies along the pleural margin, usually in the upper lobes. Because of its subpleural location, it may be associated with pneumothorax. Bullae (avascular low-attenuation areas > 1 cm in diameter) are most common with paraseptal emphysema. They may cause physiologic impairment by compressing adjacent normal lung, and uncommonly may expand to occupy more than one-third of a hemithorax (giant bullous emphysema or vanishing lung).[45]

A variety of terms have been proposed for a pattern of lung injury associated with tobacco use that consists of a histologic spectrum of respiratory bronchiolitis, emphysema, and interstitial fibrosis that does not fit the recognized forms of interstitial lung disease. These histologic terms include airspace enlargement and fibrosis (AEF),[46,47] respiratory bronchiolitis-associated interstitial lung disease with fibrosis,[48] and tobacco use-related interstitial fibrosis.[49–51] This most often is encountered as an incidental histologic finding in lung cancer resection specimens from individuals who use tobacco (Fig 12). The incidence of AEF in patients undergoing lobectomy for lung cancer is 6.5% in those with mild tobacco use and 17.7% in those with moderate tobacco use with a lower lobe predominance.[47] The fibrosis consists of paucicellular lamellar eosinophilic collagenous thickening of alveolar septa in a patchy, particularly subpleural distribution (Fig 12). It is associated frequently with respiratory bronchiolitis and emphysema. Patients generally are middle-aged, demonstrate shortness of breath, and show mixed obstructive and restrictive lung disease with markedly reduced diffusing capacity. The rate of respiratory failure in patients with AEF can be 10% in patients who also have a usual interstitial pneumonia (UIP) pattern pathologically, but it is not seen in the absence of a UIP pattern.[47]

Although AEF can present radiologically with cystic changes similar to honeycombing, mimicking UIP, its prognosis is substantially better than that of idiopathic pulmonary fibrosis (median survival, 8.8 years, compared with 4.1 years for UIP without emphysema and 3.0 years for UIP with emphysema).[52,53] AEF may be distinguished from UIP based on the presence of three or more of the tabulated features (Table 3).[49] The cysts often are clustered and confluent and often most are visible in the upper or mid-lower lobes.[52,53] Patients with AEF tend to have more emphysema than those with UIP.

Clinical Evaluation and Management

CT scan features of COPD define risk factors for lung cancer and mortality (Fig 13). Air trapping on expiratory CT scans also is associated with lung cancer risk. The presence and quantitative

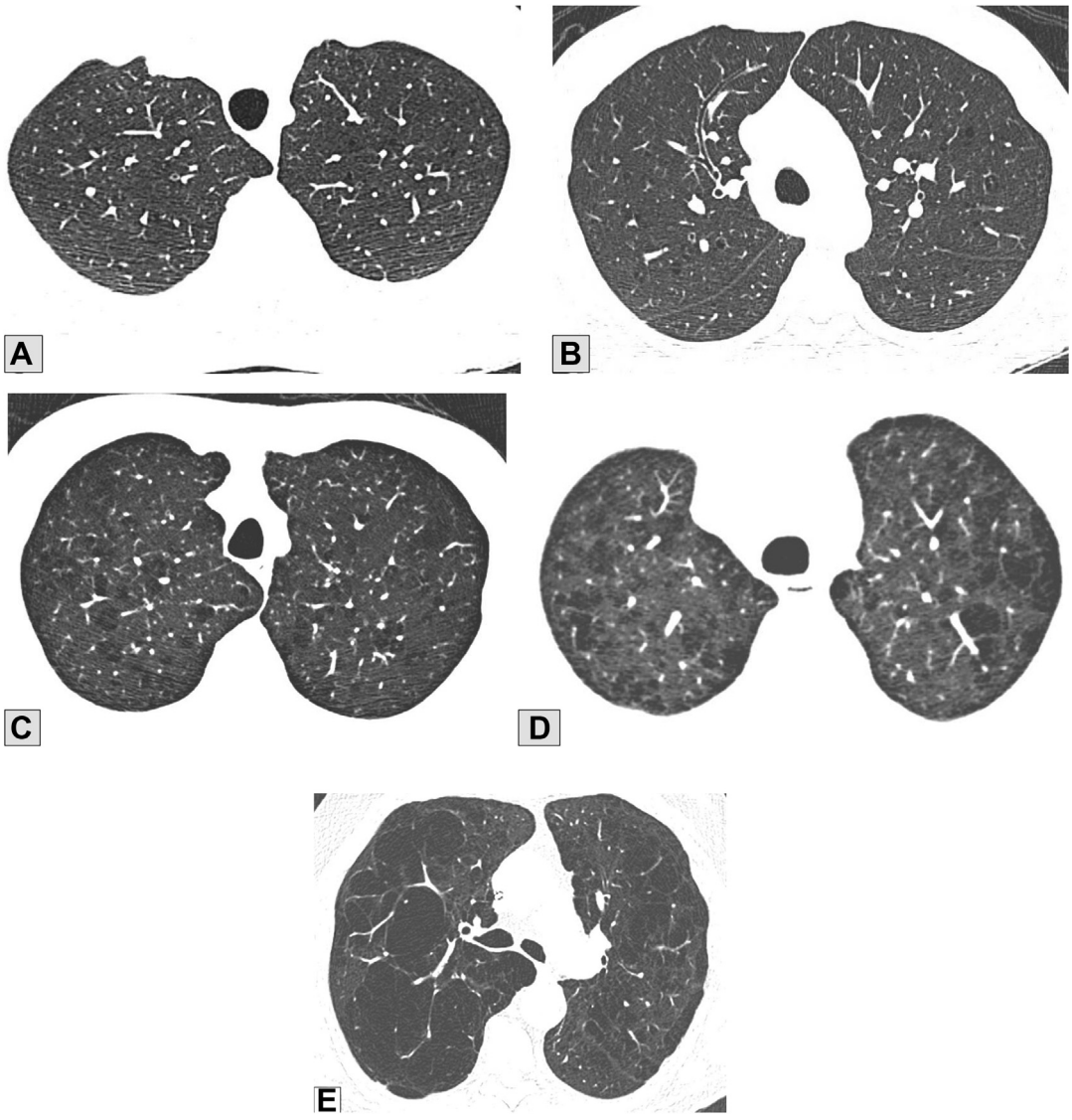

Figure 9 – *A-E, CT scans showing examples of centrilobular emphysema: trace (A), mild (B), moderate (C), confluent (D), and advanced destructive (E).*

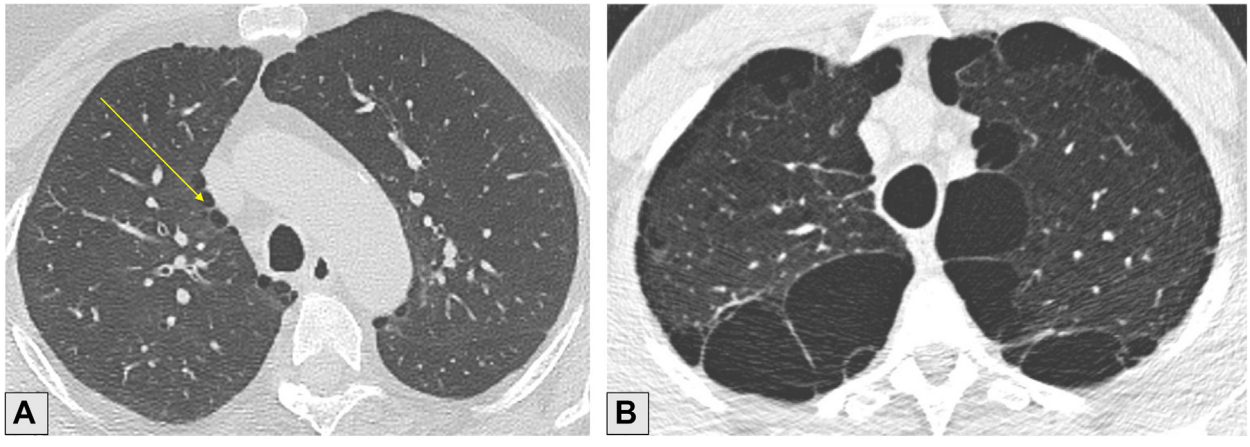

Figure 10 – *A, B, Axial CT scan images with lung windows demonstrating mild (arrow in A) and substantial (B) paraseptal emphysema.*

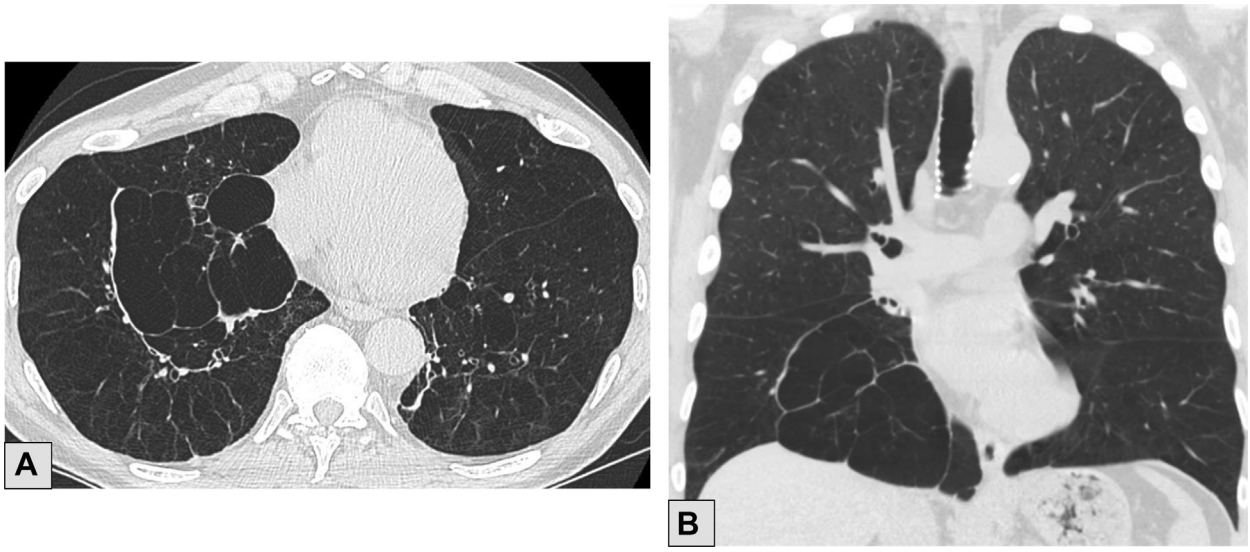

Figure 11 – *A, B, Axial (A) and coronal (B) CT scan images with lung windows showing panlobular emphysema with lower lobe predominance in a patient with α_1-antitrypsin deficiency.*

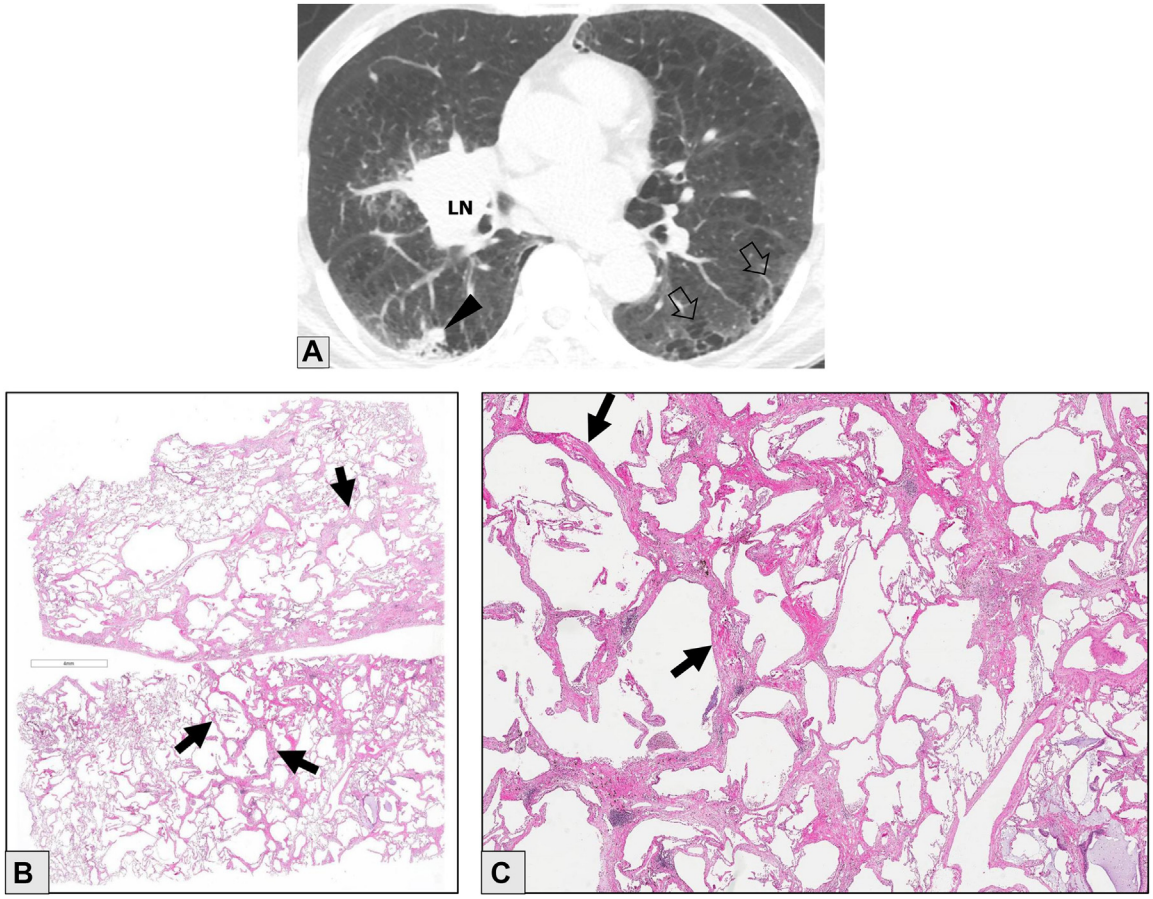

Figure 12 – *A-C, Images showing airspace enlargement and fibrosis in a patient with lung squamous cell carcinoma. A, CT scan demonstrating lung cancer (arrowhead) and right hilar lymphadenopathy (LN). Clustered subpleural cysts are present in the left lower lobe (open arrows). These cysts are distinguished from honeycombing by their asymmetry, their heterogeneous size and shape, the absence of adjacent reticulation or traction bronchiectasis, and the presence of adjacent emphysema. B, C, Photomicrographs of pathology specimens disclosing areas of airspace enlargement and alveolar wall thickening and fibrosis (arrows): low magnification (B; hematoxylin and eosin stain; original magnification, ×2) and high magnification (C; hematoxylin and eosin stain; original magnifcation, ×4). (Fig 12B and Fig 12C courtesy of Dr Joungho Han, Samsung Medical Center.)*

TABLE 3] Features Distinguishing Airspace Enlargement with Fibrosis From Usual Interstitial Pneumonia

Heterogeneous size and shape of cysts
Asymmetric cysts
Juxtasubpleural cysts, with sparing of the immediate subpleural lung
Absence of cysts in the upper lobes
Emphysema adjacent to the cystic abnormality
Absence of ground-glass opacity, reticulation, or both adjacent to cysts

severity of emphysema have been shown to be risk factors for mortality resulting from lung cancer, even in those without a clinical diagnosis of COPD.[54] It reasonably could be suggested that patients with COPD as well as those with emphysema on CT scans in the absence of a clinical diagnosis of COPD be considered for lung cancer screening, although no clinical trials support this indication. It should be pointed out that the effects of age and tobacco use history are related more strongly to lung cancer than to emphysema.[55] Additionally, the presence and severity of airflow obstruction are risk factors for lung cancer.[56]

The United States Preventive Services Task Force updated its recommendations for lung cancer screening with low-dose CT scan imaging in 2021. The age range was expanded to 50 to 80 years and the duration of tobacco use was lessened to ≥ 20 pack-years in those who currently use tobacco or have quit within the last 15 years.[57] These recommendations follow the results of the United States National Lung Screening Research Trial and the more recent Dutch–Belgian lung cancer screening trial (NELSON) trial.[58] Lung cancer screening CT scans additionally offer an opportunity to interpret existing clinical data regarding changes suggestive of COPD, coronary calcifications, thyroid abnormalities, bone mineral density, and nodules in the adrenals and to target at-risk populations.

Emphysema is relatively common in patients with pulmonary fibrosis[58] because both entities are related to tobacco use. The term combined pulmonary fibrosis and emphysema (CPFE) has been applied to this combination of findings.[59,60] CPFE has been reported in about 25% of patients with idiopathic pulmonary fibrosis[61] and in 3.1% of 2,016 asymptomatic individuals who use tobacco in South Korea.[62] The patterns of emphysema and fibrosis vary widely in different series. CPFE is clinically important because it predisposes patients to lung cancer and PH and is associated with relatively high mortality.[63–65] Also, pulmonary function evaluation can be misleading because FVC often is relatively preserved. A recent research statement from the American Thoracic Society emphasized that the definition of CPFE varies widely, with differing thresholds for the extent of emphysema and lung fibrosis.[66] The American Thoracic Society statement provides a relatively broad research definition of CPFE, requiring the presence of emphysema occupying at least 5% of total lung volume, lung fibrosis of any subtype, and a more restrictive clinical definition requiring the presence of one or more of the following: (1) emphysema occupying at least 15% of lung volume, (2) relatively preserved lung volumes and airflow with very significantly or disproportionately reduced diffusing capacity of the lungs for carbon monoxide, or (3) precapillary pulmonary hypertension unrelated to another cause. Description of the specific radiologic patterns of fibrosis and emphysema is important in characterizing CPFE (Fig 14).[66,67]

CPFE is distinguished from interstitial lung abnormalities (ILAs), which may be seen with and without emphysema.[68] ILAs are detected incidentally chest CT scan imaging abnormalities (Fig 15) suggestive of interstitial lung disease in individuals without previous diagnosis of interstitial disease.[59] ILAs are found in 3% to 17% of older adults, more commonly among those who use tobacco.[60,61] The presence of ILA is an independent predictor of mortality.[62] About 50% of ILAs progress over 5 years.[60] Because fibrotic ILA (with traction bronchiectasis or bronchiolectasis) is associated with increased likelihood of progression and mortality,[69–71] it is important for the radiologist to report the presence or absence of fibrosis.[59] In patients with lung cancer, ILAs are associated with increased

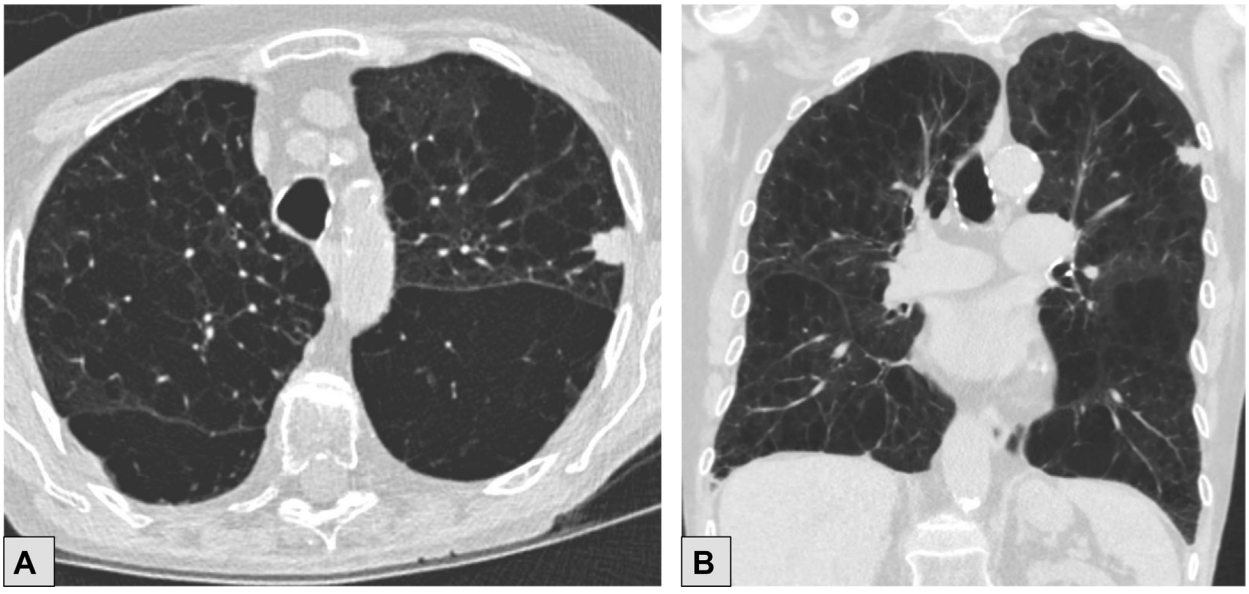

Figure 13 – *A, B, Axial (A) and coronal (B) CT scan images from a patient with severe emphysema and a 16-mm solid nodule in the left upper lobe found to be lung cancer.*

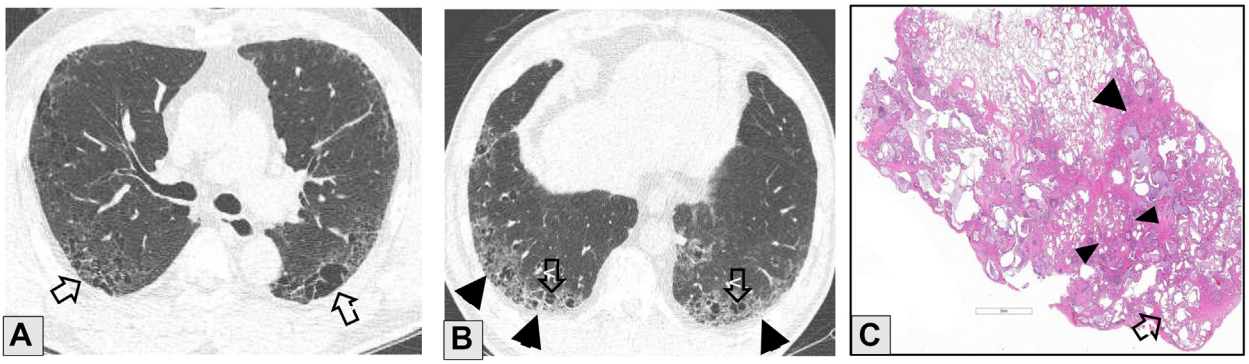

Figure 14 – *A-C, Images showing combined pulmonary fibrosis and emphysema. A, B, CT scan images showing moderate centrilobular emphysema, cysts of varying sizes (open arrows), and reticular abnormality (closed arrow), especially in the lower lungs. The larger cysts likely represent a component of airspace enlargement with fibrosis. C, Photomicrograph using hematoxylin and eosin stain (original magnification, ×2) showing dense thickening and fibrosis of interlobular septa (large closed arrow), fibrous alveolar wall thickening (small closed arrows), cellular alveolar wall inflammation, microscopic honeycomb cyst (open arrow), and emphysema. Chronically heterogeneous parenchymal fibrosis suggests the presence of usual interstitial pneumonia. (Fig 14C provided courtesy of Dr Joungho Han, Samsung Medical Center.)*

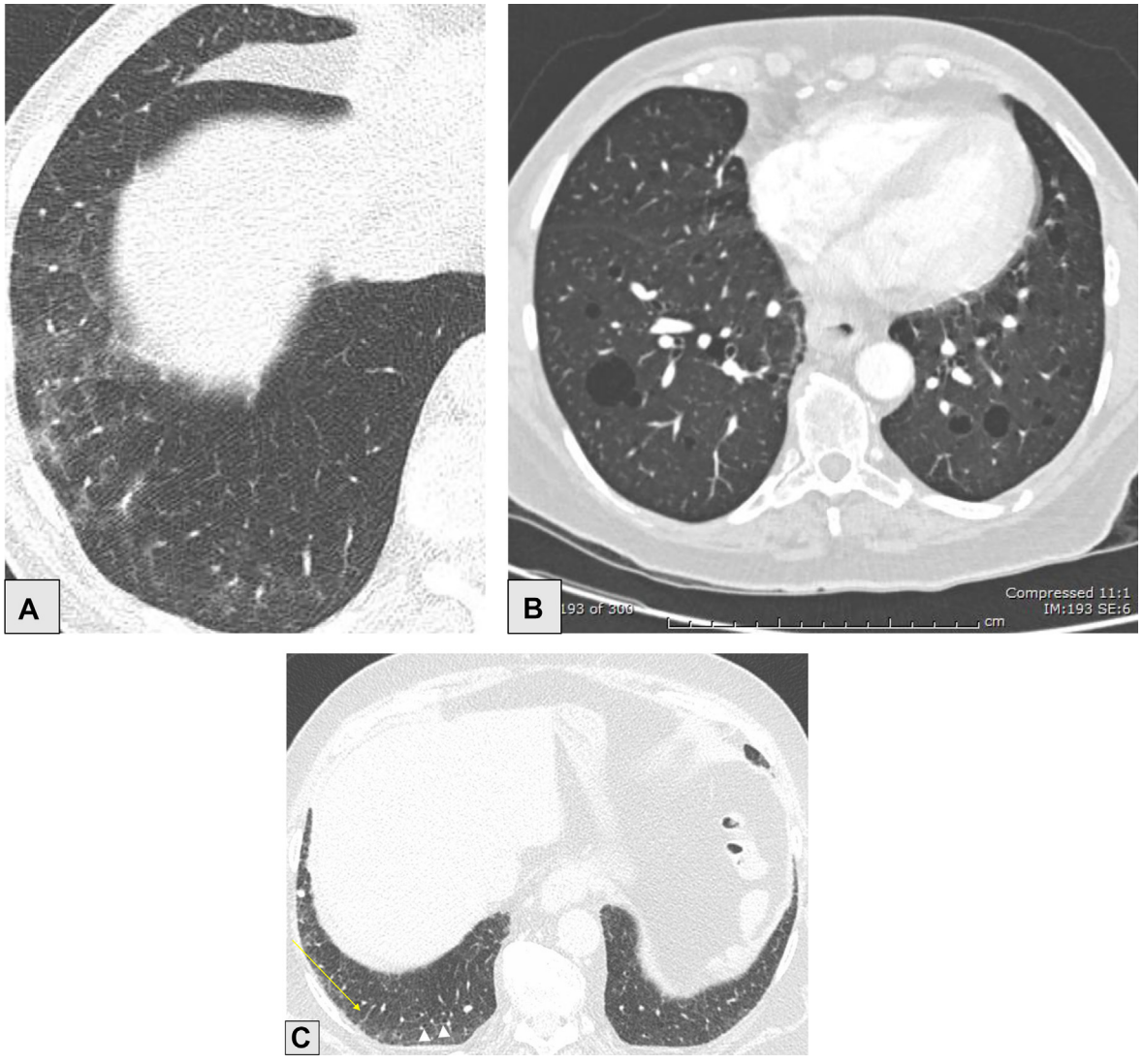

Figure 15 – *A-C, CT scans showing interstitial lung abnormality (ILA) in two different patients without suspected lung disease. A, CT scan showing nonfibrotic interstitial lung abnormality. B, Axial CT scan showing patchy ground-glass opacity in the right lower lobe and multiple well-defined cysts in both lower lobes. C, CT scan obtained through the lung bases showing fibrotic ILA: subpleural predominant reticular abnormality (yellow arrow) with traction bronchiectasis (arrowheads).*

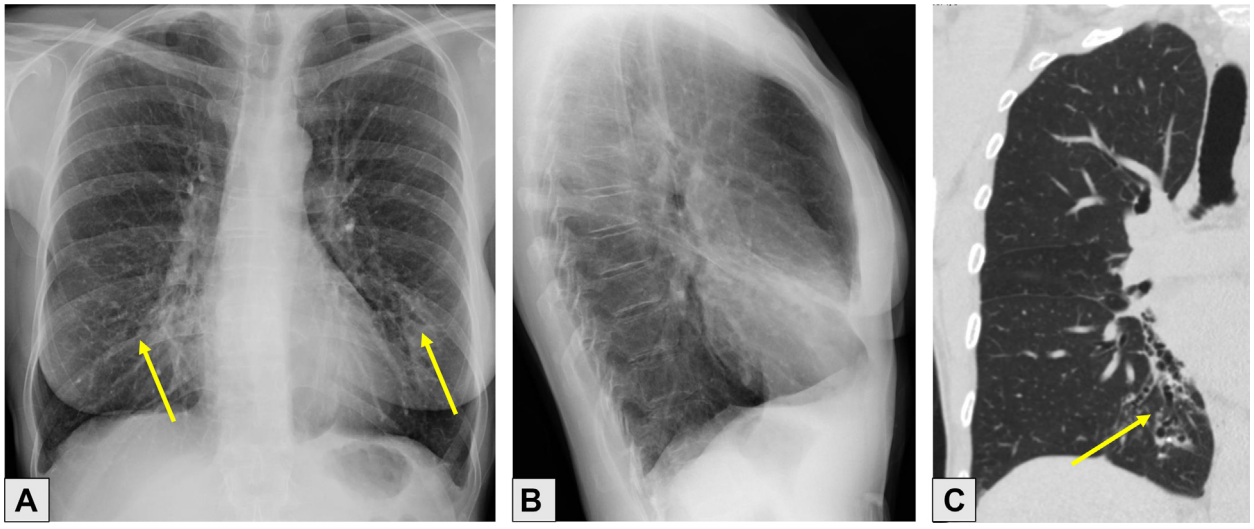

Figure 16 – *A, B, Posteroanterior (A) and lateral (B) radiographs of a patient with COPD and bronchiectasis, as demonstrated by tubular lucencies (arrows) at the lung bases. C, Coronal CT scan image (C) confirms bronchiectasis (arrow). Also note flattening of the diaphragms on the lateral radiograph (B).*

likelihood of postoperative lung injury, radiation pneumonitis, and drug toxicity.[68,72,73]

In individuals with ILA, management should include evaluation and mitigation of potential underlying causes and identification of symptoms, impaired pulmonary function, or abnormal gas exchange to suggest clinically significant interstitial lung disease. Those without current evidence of disease should be followed up regularly for progressive physiologic or symptomatic impairment.[74]

Bronchiectasis, characterized radiologically by abnormal and permanent dilatation of the bronchi, can be a comorbidity of COPD: bronchiectasis-COPD overlap syndrome. Because it is not certain that bronchiectasis-COPD overlap syndrome is a unique and distinctive clinical entity, the term COPD-bronchiectasis association[75] also has been suggested. Although our understanding of the interaction between these two inflammatory diseases remains limited, recent evidence suggests that these patients show bronchiectatic neutrophilic inflammation with an abundance of pathogenic proteobacteria and dysregulation of mucins.[76]

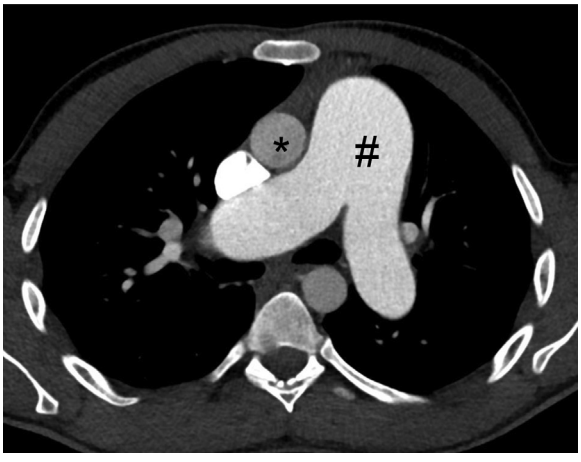

Figure 17 – *Axial contrast-enhanced CT scan image obtained at the bifurcation of the main pulmonary artery in a patient with pulmonary hypertension demonstrating a dilated (41 mm) main pulmonary artery (number sign), larger in caliber than the adjacent ascending aorta (27 mm; asterisk), suggesting pulmonary hypertension.*

It often is difficult to distinguish between COPD and bronchiectasis clinically. Both COPD and bronchiectasis may manifest as airflow obstruction. The anatomic changes of mild bronchiectasis may mimic those of chronic bronchitis. In bronchiectasis, the vicious cycle of airway infection and inflammation causes permanent structural damage to the airways, seen as abnormally dilated and thick-walled airways on high-resolution CT scan imaging. Radiologic criteria are bronchoarterial ratio of $>$ 1, lack of bronchial tapering, and visualization of peripheral bronchi within 1 cm of the pleura. Most patients with COPD with bronchiectasis show cylindrical bronchiectasis (Fig 16); only 4% will have cystic bronchiectasis.[77] Bronchiectasis is present in 20% to 60% of patients with COPD and is correlated with the severity of COPD. Patients with both bronchiectasis and COPD, compared with those with COPD alone, have increased sputum production, higher inflammatory biomarkers, worse airway obstruction, and higher exacerbation rates and all-cause mortality and are more likely to show chronic colonization by potentially pathogenic microorganisms, including *Pseudomonas aeruginosa*.[78] The management of patients with COPD with bronchiectasis has not been studied systematically.

PH, defined as a mean pulmonary artery (PA) pressure of $>$ 20 mm Hg, is a frequent and potentially morbid complication of COPD.[3] A high index of suspicion is needed for this World Health Organization group 3 PH, because many of the symptoms of PH mimic those of COPD. Transthoracic echocardiography is the initial test of choice for suspected PH because it provides an estimation of systolic PA pressure and evaluates hypertrophy and dilatation of the right ventricle.[79] However, technical difficulties are common when chest hyperinflation is present. The ratio of the main PA to ascending aorta diameter of $>$ 1 on CT scan imaging may predict PH (Fig 17).[80] Severe PH can be predicted with high sensitivity and specificity using a combination of echocardiography, N-terminal pro–B-type natriuretic peptide level, and PA to aortic diameter ratio.[81] Chest radiography may provide clues to the presence of PH

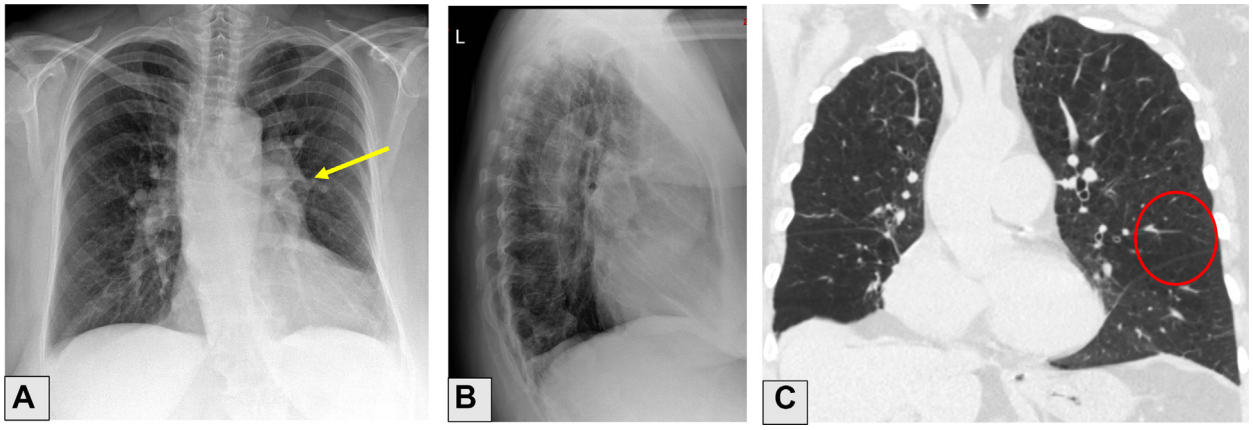

Figure 18 – *A, B, Frontal (A) and lateral (B) chest radiographs demonstrating tapering of the pulmonary vessels, also known as vascular pruning, and dilatation of the main pulmonary artery segment (arrow), consistent with pulmonary hypertension. The lungs are hyperaerated and flattening of the diaphragms is present, evident of emphysema. C, Coronal CT scan image confirming vascular pruning (red circle).*

with dilatation of the PA and its cause; increased radiolucency of the lungs, bullae, and flattening of the diaphragms suggest COPD as the cause of PH (Fig 18). A Fleischner Society statement describes the relative strengths and weaknesses of imaging methods in the noninvasive diagnosis of PH.[82] Right heart catheterization is the gold standard test to confirm the diagnosis of PH. Long-term oxygen therapy improves survival when concomitant resting hypoxemia with an oxygen saturation of $<$ 89% is present. Some patients with very severe PH may benefit from vasodilator therapy.

COPD is a multimorbid syndrome for which a broad range of pulmonary and extrapulmonary manifestations result in the heterogeneity of its clinical presentation. Extrapulmonary impairments including osteoporosis, vertebral fractures, degenerative spine disease, and arthritis often are overlooked. An investigation explored the association between COPD and both bone mineral density and vertebral fractures.[83] Almost 60% of patients showed low volumetric bone mineral density and more than one-third showed vertebral fractures. Screening for bone disease should be expanded to prevent the debilitating sequelae of bone fracture. Hip fractures as a consequence of osteoporosis add to mortality risk in COPD.[84,85]

Sarcopenia and unintentional weight loss affect up to 25% of people with COPD. CT scan imaging provides a noninvasive means of assessing skeletal muscle bulk. Cross-sectional area-based assessments of the mid-thigh, paraspinal, and pectoralis muscles have been the subject of extensive investigation.[86] Collectively, this work has demonstrated that reduced muscle size is associated with poorer clinical outcomes in people with COPD and those who use tobacco with normal lung function.[87] Lung cancer screening provides an opportunity to expand our understanding of the prevalence and clinical impact of muscle wasting.

Saber-sheath trachea (SST) is the description given to a fixed deformity of the intrathoracic trachea characterized by a reduction in the coronal diameter and an increase in sagittal diameter of the intrathoracic trachea. The tracheal index (coronal to sagittal diameter ratio measured 1 cm above the aortic arch) is less than two-thirds (Fig 19). The shape of the extrathoracic trachea is preserved. SST usually is encountered on chest CT scans performed to evaluate other disorders, but when it is observed, it should prompt investigation for other tobacco use-related findings, such as emphysema, hyperinflation, air trapping, interstitial lung disease, and lung cancer. SST is considered a sensitive and specific sign for COPD because $>$ 95% of patients with this deformity show clinical evidence of COPD.[88]

SST is reported to have a prevalence as high as 25% in patients with COPD, and the highest likelihood occurs in those with severe airflow obstruction (Global Initiative for Chronic Obstructive Lung Disease stages III-IV).[89] The cause of this deformity is not known;

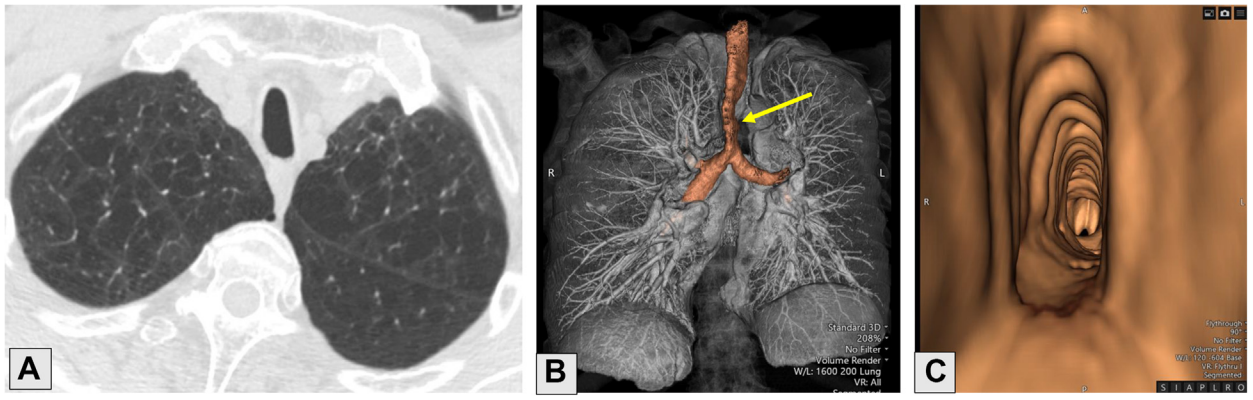

Figure 19 – *A-C, Images showing a saber-sheath trachea. A-C, Axial CT scan image with lung windows (A), multiplanar volume reformatted image (B), and virtual bronchoscopic image of trachea (C) in a patient with severe emphysema. Coronal narrowing (arrow) of the trachea with widening of the sagittal diameter are present, consistent with a saber-sheath trachea.*

mechanical forces are suspected. It has been speculated that the intrathoracic trachea is compressed by hyperinflated emphysematous lungs and high intrathoracic pressure. Rarely, this deformity has been a cause of difficult endotracheal intubation. CT scan imaging is the procedure of choice for evaluating tracheal diseases and is the most accurate method to detect SST.

Summary

Imaging, with CXR and especially CT scan imaging, provides detailed information that can characterize COPD phenotypes and can identify concurrent pulmonary disease that may estimate the natural course of disease or predict a patient's response to therapeutic intervention(s). For example, imaging plays an integral role in identifying candidates for surgical and device-based lung volume reduction.[90] Importantly, recent data also showed that CT scan imaging can detect early abnormalities, such as emphysema, air trapping, and bronchitis, that cannot be detected, even when spirometry findings are normal. CT scan imaging can help to classify emphysema into centrilobular, panlobular, or paraseptal; to detect combined pulmonary fibrosis and emphysema; and to raise suspicion for pulmonary hypertension. Recognition of these features may inform prognosis, therapy, and associated lung cancer risk. Identification of airway abnormalities, including bronchial wall thickening and mucus plugging, features suggestive of bronchitis as well as bronchiectasis and tracheal pathologic features, also may impact clinical management. The prognostic value of several extrapulmonary radiologic manifestations of disease also have been examined. Thus, radiographic imaging is a valuable tool that can provide detailed characterization of COPD, which is useful in clinical assessment and management.

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Additional information: The e-Figure is available online under "Supplementary Data."

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